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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/894,924	06/28/2001	Avi J. Ashkenazi	P1134R2C1	1667

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EXAMINER
KAUFMAN, CLAIRE M

ART UNIT	PAPER NUMBER
1646	6

DATE MAILED: 09/23/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/894,924	Applicant(s) ASHKENAZI ET AL.	
	Examiner Claire M. Kaufman	Art Unit 1646	

-- Th MAILING DATE of this communication appears on the cover sheet with the correspond nce address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *6/28/01, 8/13/01* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14 and 67-84* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14 and 67-84* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 5 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The preliminary amendments filed June 28, 2001, and August 13, 2001, have been entered.

Information Disclosure Statement

Applicants have agreed to have the Examiner enter the IDS for sister application 09/896,096 into the present application. (IDS attached.)

Priority

An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification or in an application data sheet (37 CFR 1.78(a)(2) and (a)(5)). While the instant application claims benefit to provisional applications in the first sentence, reference to parent application 09/157, 289, of which the current application is a continuation, is missing.

Specification

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The following title is suggested: Antibodies to DcR3 Polypeptide, a TNFR homolog .

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 14 and 67-83 are provisionally rejected under the judicially created doctrine of double patenting over claims 67-84 of copending Application No. 09/896,096. This is a provisional double patenting rejection since the conflicting claims have not yet been patented.

The subject matter claimed in the instant application is fully disclosed in the referenced copending application and would be covered by any patent granted on that copending application since the referenced copending application and the instant application are claiming common subject matter, as follows: the claims of 09/896,096 are encompassed by the broader claims of the instant application reciting an antibody binding DcR3.

Furthermore, there is no apparent reason why applicant would be prevented from presenting claims corresponding to those of the instant application in the other copending application. See *In re Schneller*, 397 F.2d 350, 158 USPQ 210 (CCPA 1968). See also MPEP § 804.

Claim 84 is provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of copending Application No. 09/896,096. Although the conflicting claims are not identical, they are not patentably distinct from each other because the species of antibody of claim 1 of 09/896,096 render the genus of claim 84 obvious in light of the routine, decades old, and well known methods of linking a detectable moiety (*e.g.*, fluorescent compounds) to antibodies.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode

contemplated by the inventor of carrying out his invention.

Claims 14 and 67-70 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for A) an antibody which specifically binds DcR3 polypeptide that consists of the amino acid sequence of SEQ ID NO:1 or the extracellular domain thereof consisting of at least amino acid residues 1 to 215 of SEQ ID NO:1, does not reasonably provide enablement for 1) an antibody that binds an DcR3 polypeptide which is not identical to SEQ ID NO:1 (*e.g.*, wherein the polypeptide has a sequence 80% identical to SEQ ID NO:1). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is undue include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The claims are drawn to an antibody that binds a polypeptide that is 80% identical to the the full-length or extracellular domain of SEQ ID NO:1 (DcR3) . The prior art does teach a DcR3 polypeptide (called TR4 by Emery et al., US Patent 5,885,800, and TNFR6α by Gentz et al., WO 98/30694). It also teaches several related polypeptides, for example, DR3 (Marsters et al., Curr. Biol. 6(12), 1996, #120 cited by Applicants, also called TRAMP and Apo-3 in the art) and DR4 (Pan et al., Science 276, 1997, #140 cited by Applicants, also called TRAIL-1 in the art) and DR5 (Marsters et al., Curr. Biol. 6(6), #120 cited by Applicants, also called TRAIL-2 and Apo-2). Also taught is an antibody to DR3 (Marsters et al., #120, see p. 1675, 5th paragraph, and Bodmer et al., Immunity 6, #51, see p.85, 5th paragraph), but that antibody would not be expected to bind DcR3 as the disclosed sequence of DcR3 and DR3 share little identity overall. It is acknowledged that the skill in the art is high as it relates to the discovery of TNF receptor family proteins, of which DcR3 is a member, but not as it relates to predicting sequences of the receptor proteins or, as a result, the necessary structure of an antibody that would bind an

unknown sequence of a member of the receptor family. Such an unknown sequence is encompassed by the breadth allowed with 80% identity to amino acids 1-215 or 1-300 of SEQ ID NO:1. There is no guidance for using an antibody that does not bind DcR3, which antibody is encompassed by the scope of an antibody that binds a variant protein 80% identical to SEQ ID NO:1 (DcR3) or the extracellular domain of DcR3. The structure of the antibody would be especially unpredictable for those that not only have to bind the related protein but block an activity of it.

For these reasons, it would require undue experimentation to make the claimed invention commensurate in scope with the claims.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 14, 71, 76 and 80 and dependent claims 67-70, 72-75, 77-79 and 81-84 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 14 is indefinite because it recites "binds to a DcR3 polypeptide, wherein said DcR3 polypeptide (a) has at least about 80% ... identity with ... SEQ ID NO:1...." This is confusing because it appears that by definition in the specification that a "DcR3 polypeptide" must be encoded by SEQ ID NO:2 (DNA30942, p. 5, lines 37-38), while a "DcR3 variant" is defined (p. 6, lines 17-21) as having at least about 80% ..identity with... SEQ ID NO:1...." Therefore, it appears that the claim is not using the term "DcR3" consistent with the meaning defined in the specification.

Claims 71, 76 and 80 are indefinite because of the recitation of "specifically binds". Because specificity is dependent on binding conditions and is a relative term, it introduces ambiguity into the claim. Deletion of the term "specifically" could obviate this rejection.

Priority

It is also noted that while provisional priority application 60/059,288 discloses the

complete DcR3 protein and encoding nucleic acid sequences, it does not disclose a specific utility for the protein. It is disclosed only that the protein is related to TNFR2, but no specific ligand is identified and no actual antibody is taught. Therefore, the instant application is not granted benefit of priority to 60/059,288. For the sake of prior art, the effective filing date of the instant application is that of 60/094,640, filed 07/30/98.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in-
> (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
> (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

Claims 14, 67-83 are rejected under 35 U.S.C. 102(e) as being anticipated by Emery et al. (US Patent 5,885,800, cited by applicants) as evidenced by US Patent 4,946,778.

Emery et al. teach the TR4 polypeptide (SEQ ID NO:2) which has a sequence identical to the DcR3 polypeptide (SEQ ID NO:1) of the instant application. Also taught are antibodies that bind TR4, including antibody fragments, monoclonals, polyclonals, chimeric, recombinant, and humanized antibodies, as well as methods of making the antibodies and antibody-producing host cells (col. 3, lines 22-27, and col. 10, line 58 to col. 11, line 28). Uses for such antibodies are listed and include affinity chromatography of TR4, treatment of TR4 related diseases including cancer. TR4 is disclosed as structurally related to tumor necrosis factor (TNF) receptors (*e.g.*, col. 6, lines 42-61) for which ligands, including FasL (Fas ligand) are known (col. 1, lines 31-40). The methods of making single chain recombinant antibodies are cited as disclosed in US Patent 4,946,778, cited in col. 11, line 13. Also disclosed are TR4 polypeptide antagonists which are antibodies (col. 13, lines 22-23), which necessary include antibodies that block the binding of TR4 with its ligands.

The disclosure of US Patent 4,946,778 includes techniques for production in *E. coli*, (*e.g.*, col. 35, lines 44-47) as well as yeast and mammalian host cells (col. 11, lines 12-18), and is provided as evidence of what is disclosed and is not necessary for anticipation of the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 84 is rejected under 35 U.S.C. 103(a) as being unpatentable over Emery et al. (US Patent 5,885,800, cited by applicants) and US Patent 4,946,778.

Emery et al. teach the TR4 polypeptide (SEQ ID NO:2) which has a sequence identical to the DcR3 polypeptide (SEQ ID NO:1) of the instant application. Also taught are antibodies that bind TR4 and well as methods of making the antibodies and antibody-producing (col. 3, lines 22-27, and col. 10, line 58 to col. 11, line 28). Uses for such antibodies include detection assays such as ELISA(col. 13, lines 13-39) as well as immunopreciptation (col. 13, lines 13-17). Emery does not does not teach antibodies with detectable labels.

US Patent 4,946,778 is cited by Emery et al. in col. 11, line 13 as teaching recombinant means of antibody production. US Patent 4,946,778 also teaches detectably labeled antibodies, including labeling with agents such as chemiluminescent labels (*e.g.*, col. 31, lines 59-63).

It would have been obvious to one of skill in the art at the time the invention was made to detectably label an antibody that bound TR4 using the teachings of US Patent 4,946,778 because

Emery et al. teach the usefulness of such labeled antibodies in detection assays.

Prior Art

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. WO 98/30694 (#35 cited by applicants) discloses TNFR-6α, which has the same sequence as DcR3 of the instant application and is cumulative with the reference cited above.

The art made of record and not relied upon is considered pertinent to applicant's disclosure. WO 99/14330 (#54) is not prior art, but issued from a PCT claiming priority to the two provisional applications to which the instant US application claims priority. Yu et al. (#213, J. Biol. Chem., 274(20): 13733-13736, May 1999) is not prior art, but teaches binding of DcR3 (called TR6) to FasL and LIGHT. It is suggested that "They may have a similar binding epitope for TR6 binding."

Term Usage

It is noted that the art also refers to DcR3 as TR4, TR6, TNFR-6alpha, ZTNFR-5, human NTR-1, OPG-2, FLINT#1 and hAPO6.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Claire M. Kaufman, whose telephone number is (703) 305-5791. Dr. Kaufman can generally be reached Monday through Thursday from 8:30AM to 12:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached at (703) 308-6564.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Official papers filed by fax should be directed to (703) 308-4242. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294. NOTE: If applicant *does* submit a paper by fax, the original signed copy should be retained by the applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED

so as to avoid the processing of duplicate papers in the Office. **Please** advise the examiner at the telephone number above before facsimile transmission.

Claire M. Kaufman, Ph.D.

Patent Examiner, Art Unit 1646

September 20, 2002